Since this is a provisional rejection, applicants respectfully request that the rejection be held in abeyance until allowable subject matter is indicated.

The Office rejected claims 23-47 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter, which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. The Office contends that claims 23-47 recite subject matter that is not described in the specification. The Office further contends that the specification fails to describe a representative number of species.

Applicants traverse the rejection. Lack of literal support alone is not sufficient to support a rejection under 35 U.S.C. § 112, first paragraph. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 98 (CCPA 1976). The Office has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Id.* Furthermore, M.P.E.P. § 2164.03 states:

> If applicant amends the claims and points out where and/or how the originally filed disclosure supports the amendment(s), and the examiner finds that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of the filing of the application, the examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. Accordingly, the examiner should identify what portion(s) of the amendment lack support in the originally filed disclosure, and should fully explain the basis for the examiner's finding. The examiner also should comment on the substance of applicant's remarks. Any affidavits attesting to what one of ordinary skill in the art would consider disclosed by the application as originally filed must be thoroughly analyzed and discussed in the Office action.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

Applicants' June 10, 1999, Preliminary Amendment points out where the originally filed disclosure supports the amended claims. (*See* June 10, 1999, Preliminary Amendment at 7-8.) Applicants submit that the Office has not met its burden since the Office has presented no evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.

Moreover, applicants teach the generation of multiple cell lines containing an I-*Sce*I site, including the D3 embryonic stem cell line. (Specification at 32.) Applicants teach that D3 cells are able to generate transgenic animals. (*Id.*) Applicants are not required to show an actual reduction to practice to demonstrate possession of the claimed transgenic mice. Rather, applicants' description is sufficient to show possession of the claimed transgenic animals since the skilled artisan would be able to practice the claimed invention from applicants' disclosure. *See* 64 FR 71427, 71434 (1999) (Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement).

In addition, the skilled artisan would conclude that applicants were in possession of the claimed methods, which are applicable in mice and other transgenic animals. Again, applicants are not required to show an actual reduction to practice to demonstrate possession of the claimed methods since the skilled artisan would be able to practice the claimed invention from applicants' disclosure. *See Id.*

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

Since the specification reasonably conveys to the skilled artisan that, as of the filing date, applicants were in possession of the claimed invention, applicants have fulfilled the written description requirement of 35 U.S.C. § 112, first paragraph. *See Vas-Cath Inc. v. Mahurkar*, 936 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116, (Fed. Cir. 1991). Accordingly, applicants respectfully request withdrawal of the rejection.

The Office rejected claims 23-47 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter, which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the claimed invention. The Office contends that the specification fails to provide guidance to any and all transgenic mice or animals comprising a nucleotide sequence encoding I-*Sce*I, or any and all recombinant cells provided by any and all transgenic animals. The Office alleges that the expression of transgenes in transgenic animals was not predictable at the time the application was filed.

Applicants traverse the rejection. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Furthermore, the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Id.*

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

The practice of applicants' invention requires no undue experimentation. Therefore, applicants' claimed invention is fully enabled.

Applicants teach the generation of vectors for the insertion of an I-*Sce*I site and expression of I-*Sce*I endonuclease in transgenic mice. (Specification at page 29-30, bridging paragraph; page 32, paragraph 3; page 51, paragraph 2, through page 53, paragraph 4; and Figs. 6 and 13.) Applicants teach the generation of multiple mouse cells lines containing an I-*Sce*I site, including the D3 embryonic mouse stem cell line. (Specification at 32.) Applicants teach that D3 cells are able to generate transgenic mice. (*Id.*) The generation of a transgenic mouse from D3 embryonic stem cells would require only routine experimentation. *See, e.g.*, Robertson, 1991 (Exhibit 1), at 238 ("ES cells . . . contribute to the germ line in addition to the somatic tissues, thereby enabling the use of this system as a means to generate transgenic animals.").

As evidenced by Robertson, the propagation of transgenic mice from an embryonic mouse stem cell line was well-known at the time the application was filed. The omission of descriptions of well-known techniques from a patent specification is a preferred practice. *See Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534, 3 U.S.P.Q.2d 1737, 1743 (Fed. Cir. 1987). Therefore, applicants are not required to include a description of this well known technique in the specification. Rather, applicants are permitted to teach the generation of transgenic animals using broad terminology. *See In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Accordingly, applicants submit that the specification provides adequate

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

guidance for the generation of the claimed transgenic mice. Consequently, no undue experimentation would be required to generate the claimed transgenic mice.

Furthermore, Viville, 1997, cited by the Office, indicates that the D3 line is an "excellent" embryonic stem cell line. Viville at 308, column 1, second paragraph. Although Viville indicates that creating transgenic mice is "not as easy as it looks", Viville does not indicate that anything more than routine experimentation is required to generate transgenic mice. Despite Viville pointing out that the technique is "very long and there are many steps can fail", Viville enumerates methods known in the art to achieve the successful completion of each of these steps. *See* Viville at 307-309 ("Gene targeting, Already an 'Old' Technique"). In addition, on page 319, column 2, paragraph 2, Viville states: "I am convinced that it is now possible to realise any imaginable genetic manipulation in the mouse." Nothing in Viville indicates that the generation of applicants' claimed transgenic mice would require anything more than routine experimentation. Accordingly, applicants submit that claims 23-30 and 43-45 are fully enabled.

In addition, Wall, 1996, cited by the Office, indicates that one in 33 to one in 150 injected and transferred eggs results in a transgenic mouse, rabbit, rat, cow, pig, or sheep. Wall at 61. Consequently, the skilled artisan would expect success in inserting a transgene into any of these animals without undue experimentation. Wall also indicates that transgenes are expressed in about half of transgenic lines. *Id.* Only routine experimentation would be required to define the half of the animals that express

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000

the transgene. Consequently, the skilled artisan would expect success in obtaining expression from the transgene without undue experimentation. Accordingly, applicants submit that claims 23-47 are fully enabled, and respectfully request withdrawal of the rejection.

Furthermore, the expression of a transgene is not required for the incorporation of an I-*Sce*I site in claims 28-42, 46, and 47. The detection of incorporated I-*Sce*I sites by Southern blotting is described on pages 32-38 of the specification. Therefore, the insertion of an I-*Sce*I site in a chromosome of a transgenic animal can be readily determined by Southern blotting, without the expression of the transgene. Accordingly, applicants submit that claims 28-42, 46, and 47 are fully enabled, and respectfully request withdrawal of the rejection.

Applicants submit that this application is now in condition for allowance. If the Examiner should disagree, the Examiner is invited to contact the undersigned to discuss any remaining issues.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER L.L.P.

By: Leslie McDonell (Reg. No. 34,872)
for: Kenneth J. Meyers
Reg. No. 25,146

Dated: January 27, 2000

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, D. C. 20005
202-408-4000